

## Remarks

Reconsideration of the present Application is respectfully requested.

In the Office Action of August 14, 2006, the Examiner raised several objections and rejections that are summarized below.

### I. Summary of Office Action

The Examiner has rejected Claims 13-17 under 35 U.S.C. section 102(b) as anticipated by or, in the alternative, under 35 U.S.C. section 103(a) as obvious over either Weissgurber (German Patent Number 19,914,358 A1) or Weissgurber (German Patent Number 19,914,358 C2) in view of Weissgurber (US Patent Number 6,627,075), where Weissgurber '075 serves as a translation of Weissgurber '358 A1 and Weissgurber '358 C2.

The Examiner has further rejected claims 13-17 under 35 U.S.C. section 103(a) as unpatentable over either Weissgurber (German Patent Number 19,914,358 A1) or Weissgurber (German Patent Number 19,914,358 C2) in view of Weissgurber (US Patent Number 6,627,075) and either Spraul (US Patent Number 6,402,946) or Zimmerman (European Patent Number 1,248,096), where Weissgurber '075 serves as a translation of Weissgurber '358 A1 and Weissgurber '358 C2.

Applicants shall address each of the objections and rejections in the Discussion that follows.

### II. Discussion

#### A. Novelty

The Examiner contends that claims 13-17 are unpatentable over either Weissgurber (German Patent Number 19,914,358 A1) or Weissgurber (German Patent Number 19,914,358 C2) in view of Weissgurber (US Patent Number 6,627,075), where Weissgurber '075 serves as a translation of Weissgurber '358 A1 and Weissgurber '358 C2 as the claims are considered to read directly onto the citations. Applicants respectfully request that the Examiner reconsider his position. Applicants shall consider independent claim 13 first.

Independent claim 13 recites a method for measuring nano-scale flow rates of a liquid in a high pressure liquid chromatography (HPLC) system comprising :

measuring the a main flow rate in a main flow path between an HPLC pump and a flow divider,

dividing said main flow path into an operating flow path and a waste flow path according to a split ratio of said flow divider,

measuring a waste flow rate in said waste flow path,

subtracting said waste flow rate from said main flow rate to determine a flow rate difference,

dividing said flow rate difference by said main flow rate to determine an empirical split ratio.

A complete reading of Weissgurber '075 shows that there is no anticipation of claim 13.

Hybritech Inc. v Monoclonal Antibodies Inc. 802 F.2d 1367, 231 U.S.P.Q. 81,90 (Fed. Cir. 1986) provides that;

"It is axiomatic that for prior art to anticipate under 102 it has to meet every element of the claimed invention, and that such a determination is one fact."

Not one of the three main embodiments (as shown in Figs 1-3) or the calibration system (as shown in Fig 4) of Weissgurber '075 provides a means for both measuring flow in the "main flow path" and the "waste flow path". Therefore, no method of using these devices can include the steps of measuring the flow in a "main flow path" and a "waste flow path", as described by the present claim 13. Furthermore, if these elements are not fulfilled by Weissgurber '075, then there can be no "subtracting [of] said waste flow rate from said main flow rate to determine a flow rate difference", nor, as the Examiner agrees, a "dividing [of] said flow rate difference by said main flow rate to determine an empirical split ratio." At best, Weissgurber '075 fails to describe three essential elements of the method recited in claim 13. As such the Applicants submit that there is nothing at issue under 35 U.S.C. section 102.

#### B. Obviousness

The Examiner contends that claims 13-17 under 35 U.S.C. section 103(a) are unpatentable over either Weissgurber (German Patent Number 19,914,358 A1) or Weissgurber (German Patent Number 19,914,358 C2) in view of Weissgurber (US Patent Number 6,627,075), where Weissgurber '075 serves as a translation of Weissgurber '358 A1 and Weissgurber '358 C2. The Examiner suggests that any difference between the claims and Weissgurber '358 A1 or Weissgurber '358 C2 in view of Weissgurber '075, reside merely in optimizing the elements of the cited art.

As described above, the Applicants submit that there are at least three elements recited in the present claim 13 that are not provided by Weissgurber '075. Furthermore, the effect of the method of claim 13 is quite different to that provided by Weissgurber '075.

Applicants refer to Weissgurber '358 A1 at page 5 lines 4-5, highlighting that "[it] describes an elaborate calibration procedure that must be used". The invention as presently claimed requires no calibration to compensate for

solvent composition gradients typically used in HPLC, which the Applicants state as a particular advantage at page 5 lines 22-24.

Applicants submit that not only does claim 13 recite at least three steps that are not even alluded to in Weissgurber '075, but that these steps enable the distinct advantage of the elimination of a time-consuming and costly calibration step. This is not provided by optimizing elements of Weissgurber '075. It is not possible to optimize steps that are not present.

The Examiner also contends that claims 13-17 are unpatentable under 35 U.S.C. section 103(a) over either Weissgurber (German Patent Number 19,914,358 A1) or Weissgurber (German Patent Number 19,914,358 C2) in view of Weissgurber (US Patent Number 6,627,075) and either Spraul (US Patent Number 6,402,946) or Zimmerman (European Patent Number 1,248,096), where Weissgurber '075 serves as a translation of Weissgurber '358 A1 and Weissgurber '358 C2. The Examiner contends that the claims differ from Weissgurber '075 only in reciting the calculating the split ratio. Spraul '946 discloses split ratios of splitters between chromatography columns and detectors vary their ratios to provide an exact flow. Zimmerman '096 discloses that splitters for dividing chromatographic flows into excess and working fluid streams may be preset or varied. The Examiner contends that it would have been obvious to calculate the split ratio in Weissgurber '075 in view of either Spraul '946, because Spraul '946 discloses split ratios of splitters between liquid chromatography columns and detectors vary their ratios to provide an exact flow, or Zimmerman '096 because Zimmerman '096 discloses that splitters for dividing chromatographic flows into excess and working fluid streams may be preset or varied.

The mandates in *Graham v Deere* that have been consistently applied by the courts require that the claimed invention be considered as a whole, any references must be considered as a whole and suggest desirability and thus obviousness of making the combination, the references ought to be viewed without hindsight, and "ought to be tried" is not the test for obviousness.

As Applicants describe above, Weissgurber '075 lacks teaching of the steps of measuring of either a main flow rate in a main flow path or a waste flow rate in a waste flow path, subtracting the waste flow rate from the main flow rate to determine a flow rate difference, and dividing the flow rate difference by the main flow rate to determine an empirical split ratio.

Spraul '946 describes an apparatus for dividing the output of a liquid chromatography system into two separate detectors. The Examiner states correctly that, at column 8 lines 3 to 7, Spraul '946 teaches "The splitter can be fixed or free adjustable. The splitter must only meet the requirements to split the flow coming from the flow source in a suited ratio and to provide an exact flow after the split". However, Spraul '946 teaches little more about the splitter itself, without referring to how the ratio might be varied – only that it can be. There is no measurement of the flow in the "main flow" upstream of the splitter. Likewise there is no waste flow, and thus no measurement of a waste flow. Moreover, there is no actual calculation of an empirical split ratio

by any means, let alone the Applicants' claimed method. Applicants submit that Spraul '946 adds nothing to Weissgurber '075 and as such that the Examiner's objection based on this reference is unsustainable.

Zimmerman '096 describes an apparatus for dividing flow at adjustable flow rates. Like Spraul '946 however, Zimmerman '096 fails to disclose the features of the present claim 13 that are missing from Weissgurber '075. Zimmerman '096 teaches no measurement of the flow in the "main flow" upstream of the splitter. Though there is disclosure of the measurement of flow in the waste flow, there is no calculation of an empirical split ratio as described in the present claim 13. The waste flow rate is not subtracted from the main flow rate, and the result is not divided by the main flow rate to give the empirical split ratio.

Individually or combined, none of the references cited by the Examiner teach all elements of the present claim 13. Moreover, Applicants respectfully submit that none of the references cited suggest or infer that the additional elements described in claim 13 could be either successful or desirable. In the absence of such direction, Applicants submit that any rejection of the present claim 13 over the cited documents is based on mere hindsight.

Applicants respectfully submit that present claim 13 is both novel and non-obvious over the cited art. By virtue of their dependency on claim 13, Applicants submit that claims 14 to 17 are novel and non-obvious over the cited art.

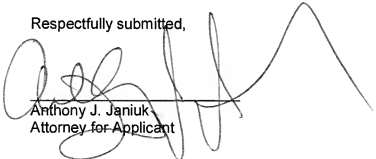
### III. Conclusion

Applicants respectfully submit the present Application is in condition for allowance which action is earnestly solicited. Should the Examiner have any additional concerns regarding the allowance of this application, he is invited to contact the undersigned to further expedite the application.

Respectfully submitted,

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